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*Published in:*  
Journal of Clinical Periodontology

*DOI:*  
[10.1111/jcpe.13055](https://doi.org/10.1111/jcpe.13055)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Final author's version (accepted by publisher, after peer review)

*Publication date:*  
2019

[Link to publication in University of Groningen/UMCG research database](#)

### *Citation for published version (APA):*

Raghoobar, G. M., Onclin, P., Boven, G. C., Vissink, A., & Meijer, H. J. A. (2019). Long-term effectiveness of maxillary sinus floor augmentation: A systematic review and meta-analysis. *Journal of Clinical Periodontology*, 46, 307-318. <https://doi.org/10.1111/jcpe.13055>

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Article type : Supplement Article

## **Long-term effectiveness of maxillary sinus floor augmentation A systematic review and meta-analysis**

**Running title:** Sinus lift interventions

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**Key words:** sinus lift; bone augmentation; dental implants; lateral approach; biological complications; maxillary sinus floor elevation; systematic review; meta-analysis

### **Conflict of interest and sources of funding statement**

The authors have stated explicitly that there are no conflicts of interest in connection with this article and no funding was received.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jcpe.13055

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## Abstract

**Aim:** To assess the long-term effectiveness ( $\geq 5$  years) of maxillary sinus floor augmentation (MSFA) procedures applying the lateral window technique and to determine possible differences in outcome between simultaneous and delayed implant placement, partially and fully edentulous patients, and grafting procedures.

**Materials and methods:** MEDLINE (1950–May 2018), EMBASE (1966–May 2018) and Cochrane Central Register of Controlled Trials (1800–May 2018) were searched. Inclusion criteria were prospective studies with follow-up  $\geq 5$  years and a residual bone height  $\leq 6$  mm. Outcome measures included implant loss, peri-implant bone level change, suprastructure survival, patient-reported outcome measures and overall complications. Data were pooled and analyzed using a random effects model.

**Results:** Out of 2873 selected articles, 11 studies fulfilled all inclusion criteria. Meta-analysis revealed a weighted annual implant loss of 0.43% (95% CI: 0.37%-0.49%). Meta-regression analysis did not reveal significant differences in implant loss neither between edentulous and dentate patients, nor implants placed simultaneously with or delayed after MSFA, nor implants placed in MSFA using solely autologous bone or bone substitutes. The results of the other outcome measures were favorable and overall complications were low.

**Conclusion:** MSFA is a reliable procedure in the partially and fully edentulous maxilla for support of dental implants..

## CLINICAL RELEVANCE

### *Scientific rationale for the study:*

Little evidence is available on 5-years effectiveness of maxillary sinus floor augmentation (MSFA) procedures applying the lateral window technique for implant placement in patients.

### *Principal findings:*

The weighted annual implant loss was 0.43%. No significant differences regarding implant loss rate were found between edentulous and dentate patients neither between areas reconstructed with autogenous bone or bone substitutes nor between 1- or 2- stage surgery.

### *Practical implications:*

MSFA is a reliable treatment for patients with partially and fully edentulous maxillae. Most eligible studies were performed at specialized clinics. It is unclear whether similar results can be achieved in daily practice.

## Introduction

Implant-supported fixed and removable prostheses are common, successful treatments to replace missing teeth with reliable long-term results (Buser, Sennerby, & De Bruyn, 2017). However, implant placement in the posterior maxilla remains a challenge due to the frequent lack of bone for reliable placement. This lack of bone is caused by alveolar ridge resorption and maxillary sinus

pneumatization. To deal with this challenge, a variety of pre-implant surgical and alternative treatment solutions have been proposed, including maxillary sinus floor elevation combined with grafting procedures (Aghaloo, Misch, Lin, Iacono, & Wang, 2016). As an alternative to such grafting procedures, others have used short implants (Thoma, Zeltner, Husler, Hammerle, & Jung, 2015), tilted implants in the anterior maxilla and zygoma implants to circumvent the limited bone height (Esposito et al., 2010).

To reconstruct a resorbed posterior maxilla and to partially occlude a pneumatized maxillary sinus, a variety of maxillary sinus floor augmentation (MSFA) techniques have been developed. In MSFA using the lateral window technique (Boyne & James, 1980; Tatum, 1986), the space created between the residual maxillary ridge and elevated Schneiderian membrane is filled with a grafting material. MSFA is implemented as either a pre-implant surgical procedure or is combined with implant placement when the implant can be placed with sufficient primary stability. Favourable outcomes regarding implant survival have been reported in a number of systematic reviews including those of Pjetursson, Tan, Zewahlen, & Lang, (2008), Esposito et al., (2010), Corbella, Taschieri, & Del Fabbro, (2015), Thoma et al., (2015), Danesh-Sani, Engebretson, & Janal, (2017), Ting, Rice, Braid, Lee, & Suzuki, (2017) and Starch-Jensen et al., (2018).

Autogenous bone (AB), bone substitutes (BS), and a mixture of AB and BS are the most commonly used grafting materials. More recently, several studies showed that successful bone formation can also be obtained by simply only elevating the maxillary sinus membrane using a lateral or transcrestal approach combined with immediate implant placement (Lundgren et al., 2017; Moraschini, Uzeda, Sartoretto, & Calasans-Maia, 2017; Starch-Jensen & Jensen, 2017).

For AB, the most common extra-oral donor sites are the iliac crest and calvaria (Kuik et al., 2016). Common intra-oral donor sites include the maxillary tuberosity, zygomatico-maxillary buttress, zygoma, mandibular symphysis, and the mandibular corpus or ramus (Raghoobar, Meijndert, Kalk, & Vissink, 2007). As harvesting AB is accompanied by donor site morbidity, BS have been proposed as an alternative grafting material (Al-Nawas & Schiegnitz, 2014). While AB is osseointegrative and osseointegrative, most BS materials are mainly osseointegrative (Al-Nawas & Schiegnitz, 2014). AB provides strong activation of bone formation. This difference in bone-forming capacity is reflected by the longer healing times that are commonly assumed when performing a MSFA with BS (Lundgren et al., 2017). Regarding implant survival following MSFA, one systematic review concluded that rough surface implants placed in particulated AB have a significantly lower annual implant failure rate compared with BS in MSFA (Pjetursson et al., 2008). A more recent systematic review did not confirm this conclusion (Al-Nawas & Schiegnitz, 2014; Starch-Jensen et al., 2018).

As bone formation takes time, particularly when BS are used, the effect of adding biologicals to AB, and in particular to BS, has been studied. Studies have suggested that adding growth factors to AB and BS enhances early bone formation and bone-to-implant contact (Kelly, Vaughn, & Anderson, 2016; Pocaterra et al., 2016). Autogenous growth factors, human recombinant growth factors and other

bone-stimulating agents are presumed to act as catalysts for bone formation, but their use is still controversial.

Previous systematic reviews concluded that short-term survival rates of dental implants after MSFA, irrespective of the grafting material applied, are very high (Pjetursson et al., 2008; Nkenke & Stelzle, 2009; Jensen et al., 2013; Corbella et al., 2015). The optimal grafting material to ensure long-term survival of implants still has to be determined, however. Based on sparse data, it was reported that the 5-year implant survival after MSFA with AB was 97% compared to 95% for deproteinized bovine bone mineral (DBBM) (Starch-Jensen et al., 2018). It has to be stressed that the various systematic reviews did not separately discuss implant survival in fully and partially edentulous patients. The latter might be of importance, as a comparative study (Raghoobar, Timmenga, Reintsema, Stegenga, & Vissink, 2001) showed that implant survival rates differed between partially dentate (97.0%) and fully edentulous maxillae (90.8%).

Tonetti & Hammerle (2008) emphasized the need to answer comparative questions to establish the clinical benefit of bone augmentation procedures using various techniques as well as the need to determine their effectiveness, adverse effects, long-term outcomes, morbidity, patient satisfaction and cost. This conclusion was based on few trials, usually underpowered, with short follow-up periods. Long-term efficacy of AB compared to BS regarding implant survival was not reported. Therefore, the objectives of the current review were to assess the  $\geq 5$ -years effectiveness of MSFA procedures that use the lateral window technique as well as to assess differences in outcome between simultaneous and delayed implant placement, partial or fully edentulous patients and various grafting procedures.

## Material and Methods

### Protocol development

A protocol was developed *a priori* to answer the following question: *What is the  $\geq 5$ -years effectiveness of MSFA procedures that use the lateral window technique and are there differences in outcome between simultaneous and delayed implant placement, partial or fully edentulous patients and various grafting procedures?* The protocol fulfilled the PRISMA-P 2015 checklist (Shamseer et al., 2015).

### Search strategy and study selection

A thorough search of the literature was conducted with help of a biomedical specialist (completed May 15, 2018). The primary database was Medline (via PubMed). Additional databases used were Embase and The Cochrane Central Register of Controlled Trials. The automated search was supplemented by manually searching the references of relevant review articles and eligible studies for additional useful publications. The search strategy was a combination of a Mesh term and free text words. "Sinus Floor Augmentation"[Mesh] OR Sinus Floor Augmentation[tiab] OR sinus lift\*[tiab] OR sinus augmentation\*[tiab] OR sinus floor augmentation[tiab] OR sinus floor elevation\*[tiab] OR sinus graft\*[tiab] OR maxillary augmentation [tiab]. No language restriction were applied.

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## Eligibility criteria

To be eligible, the following criteria (PICO) should be met:

1. *Type of Patients or population:* edentulous or dentate patients in good general health, requiring MSFA (lateral window technique) for simultaneous or delayed implant placement and who presented with a mean residual bone height underneath the maxillary sinus at the site of the implant placement  $\leq 6$ mm.
2. *Type of Intervention:* MSFA with a mixture of AB and BS, or solely BS or application of biologicals, or no graft material;.
3. *Comparison or control group:* MSFA with AB
4. *Outcomes:* Primary outcome: implant loss. Implant loss was defined as the percentage of implants initially placed that were lost at follow-up. Secondary outcomes: peri-implant bone level change, suprastructure survival, patient-reported outcome measures (PROMs) and technical and biological complications.
5. *Study design:* randomised clinical trials (RCTs) with a follow-up  $\geq 5$  years. Prospective controlled clinical trials (CCTs), cohort studies and case series with  $\geq 5$  years of follow-up after functional loading and  $\geq 10$  patients per intervention/treatment group were also considered eligible for inclusion in case no RCTs were available.

## Screening methods

Titles and abstract of the searches were screened by two independent reviewers (G.M.R.&P.O.). Full-text documents were obtained for all articles meeting the inclusion criteria. Next, full text analysis was obtained for independent risk of bias assessment performed by the two reviewers (G.M.R.&P.O.).

Methodological quality of randomized studies was assessed using the Cochrane Collaboration's tool for assessing risk of bias (Higgins & Green, 2011). Six main quality criteria were assessed: sequence generation, allocation concealment, blinding treatment outcomes to outcome examiners, completeness of follow-up, selective outcome reporting and other sources of bias.

The methodological quality of non-randomized studies was assessed using MINORS (Slim et al., 2003) as the Cochrane Collaboration's tool is not suitable for non-randomized studies. MINORS contains twelve quality criteria, assessing aim, inclusion of patients, data collection, blinding treatment, follow-up, analysis and, when applicable, comparison between groups.

The risk of bias was interpreted and ranked as low, medium or high. In case of disagreement, consensus was reached by discussion, if necessary in consultation with a third reviewer (H.J.A.M).

## Data extraction

The following data were extracted: author(s), year of publication, study design, number of patients, mean age, partially or fully edentulous jaw, number of sinus lifts, residual bone height of the alveolar process under the sinus before implant placement, augmentation material (AB and/or BS, no grafting

material), use of membranes, implant placed simultaneously or delayed, lateral sinus approach, type of restoration (fixed restoration or overdenture), follow-up in months, survival rate of implants and restorations, marginal bone level changes, PROMs, intraoperative complications (e.g., Schneiderian membrane perforation, bleeding), postoperative complications (e.g., sinusitis, infection, total graft loss), and prosthetic complications.

### **Statistical analysis**

Data on implant loss rate, simultaneous or delayed implant placement, grafting material, and maxillary dental status (edentulous versus dentate) were pooled and analyzed using Comprehensive Meta-Analysis software, Version 3 (CMA, Biostat, Englewood, NJ 07631, USA). A random effects model was used to calculate weighted event rates and corresponding 95% confidence intervals (CI). Statistical heterogeneity amongst studies was assessed with  $I^2$ . To analyze sources of heterogeneity between studies, meta-regression analysis (random effects model) was performed with studies reporting number of surgical stages (simultaneous vs delayed implant placement), type of grafting material (AB versus BS versus mixed) and type of maxillary dental status. Publication bias was assessed applying funnel plots.

## **Results**

### *Study selection*

The primary search resulted in 2389 hits for Medline, 362 hits for Embase search and 122 hits for Cochrane search (Figure 1). In total 2873 papers were identified, of which 495 articles were duplicates or review articles. These papers were excluded. Two additional records were identified by manually searching the reference lists. After title and abstract screening, another 2340 papers were excluded because they did not meet the inclusion and exclusion criteria, leaving 38 papers to be evaluated by full-text analysis. The initial interrater agreements on title/abstract selection and after reading full-text were 87% and 95%, respectively. Disagreements ( $n=2$ ) were due to slight differences in interpretation and were easily resolved in a consensus meeting. Authors of 11 articles did not respond to an email concerning queries regarding the groups they mentioned in their articles and had to be excluded because of missing data. Another study was excluded (Hallman & Zetterqvist, 2004) because the same patient sample, now with a 10-year observation period, was reported in another included publication (Mordenfeld, Albrektsson, & Hallman, 2014). None of the studies were RCT's directly answering the PICO question. Nevertheless, eleven prospective cohort studies with a sufficient quality were finally included in this systematic review to get insight in the influence of graft materials, timing of implant placement and edentulous/dentate situation.



### *Treatment modalities*

In total 383 patients, 615 MSFA procedures and 1517 implants were included (Table 1). Three studies excluded smokers, five studies included smokers and three studies lacked details on smoking status. The approach to the lateral antral wall was performed by a trap door technique and/or by preparing an access hole by removal of the buccal bone plate (Table 1). AB was harvested from the maxillary sinus region (Bornstein, Chappuis, Von Arx, & Buser, 2008; Khoury, Keller, & Keeve, 2017), chin (Bornstein et al., 2008; Mordenfeld et al., 2014), tuberosity (Cannizzaro et al., 2013; Khoury et al., 2017), ascending mandibular ramus (Bornstein et al., 2008; Khoury et al., 2017), anterior iliac crest (Boven, Slot, Raghoobar, Vissink, & Meijer, 2017; Dasmah, Thor, Ekestubbe, Sennerby, & Rasmusson, 2013; Slot, Raghoobar, Cune, Vissink, & Meijer, 2018) or posterior iliac crest (Bornstein et al., 2008). Deproteinized bovine bone mineral (DBBM; Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) was used in six studies (Bornstein et al., 2008; Cannizzaro et al., 2013; Mordenfeld et al., 2014, 2016; Oliveira, El Hage, Carrel, Lombardi, & Bernard, 2012; Özkan, Akoğlu, & Kulak-Özkan, 2011) and synthetic BS (Ceros TCP, Mathys AG, Bettlach, Switzerland and BoneCeramic, Straumann AG, Basel, Switzerland) in two studies (Bornstein et al., 2008; Mordenfeld et al., 2016). In one study, alloplastic grafts were used in combination with AB (Khoury et al., 2017): AB bone chips in the basal part close to the alveolar crest and phycogenic hydroxyapatite (Algipore, Dentsply Sirona, Mannheim, Germany) cranially close to the elevated sinus membrane (Khoury et al., 2017). When implants were placed simultaneously with MSFA, the entire surface of the implants was covered by AB. In one study, no graft was used (Cricchio, Sennerby, & Lundgren, 2011). A variety of mixtures of AB and BS was compared in four studies, while BS alone was assessed in three studies, and AB alone in the other three studies. In four studies the window was covered with a resorbable membrane and in one study with a nonresorbable titanium membrane (Table 1). In four studies no membranes were used of which in two studies AB blocks were fixed on the lateral wall to reconstruct the bone width and thus covered the window (Boven et al., 2017; Slot et al., 2018). In one study, the lateral bone window was removed and repositioned after MSFA and placement of the implant (Cricchio et al., 2011). In the remaining two studies, it was unclear whether a membrane was used.

Various implant systems were used (Table 1). Immediate implant installation was performed in four studies with a healing period ranging from 45 days to 6 months. In delayed approaches, the healing period for the graft material ranged between 3 to 18 months (Bornstein et al., 2008; Oliveira et al., 2012; Dasmah et al., 2013; Mordenfeld et al., 2014; Mordenfeld et al., 2016; Khoury et al., 2017; Boven et al., 2017; Slot et al., 2018). The prosthetic constructions were fixed restorations in nine studies and overdenture with bar-connection in two studies. Final prosthetic rehabilitation was performed three to six months after implant installation.



### **Methodological quality**

The quality of the eligible studies ranged from medium to high. Overall, the non-randomised studies were inadequate in blinding procedures and study size calculation, which was the main cause for the medium and high risk of bias ratings (Supplementary figure 1). Loss-to-follow-up appeared to >5% in most cases. For the RCTs the risk of bias was low to medium (Supplementary figure 2). None of the three studies followed a strict blinding procedure. The study of Mordenfeld et al. (2016) was rated as having a medium risk of bias although the selection and randomization of patients were not reported. It was rated as medium risk because overall the study was well described.

### **Outcome measures**

5-year implant survival ranged from 88.6% to 100% (Table 2). Implant loss was significantly higher when a mix of AB and BS was used (see meta-analysis for details). Implant survival showed neither a significant difference between fully and partial edentulous patients nor between one- and two-stage surgery.

Adding platelet-rich plasma to AB did not result in less resorption of the grafting material (Dasmah et al., 2013). Mean marginal bone loss between baseline and last follow-up was limited in all studies (Table 2). Of note, peri-implant marginal bone loss in areas grafted with AB, a mixture of AB and BS, or BS alone was not compared within the same study in any of the included studies.

Patients' appreciation of the implant treatment outcome after MSFA was favourable but only assessed in two studies (Table 2).

Intra- and postoperative complications after MSFA were minor and unrelated to the grafting material used (Table 2). Postoperative wound healing was generally uneventful notwithstanding the rather frequent occurrence of sinus membrane perforations, ranging from 0% to 31.5%. Commonly, smaller perforations were left untreated, while larger perforations were sealed with fibrin sealant, collagen fleece, a resorbable collagen membrane or bone blocks.

Long-term prosthetic complications were mostly reported as minor which could be repaired chair-side. In five patients prosthetic complications resulted in fabrication of a new construction (Table 2).

### *Meta-analysis*

$I^2$  was higher than 90%, indicating considerable heterogeneity. One study was not included in the meta-analysis on grafting materials because as no grafting material was used (Cricchio et al., 2011). Three studies were not included in the meta-analysis on dental status as insufficient data on dental status were described in these papers (Cannizzaro et al., 2013; Mordenfeld et al., 2014; Mordenfeld et al., 2016).

Overall cumulative weighted average annual implant loss was 0.43 (95% CI 0.38-0.49;  $I^2=99.53\%$ ) representing a 5-years implant survival rate of 97.8% (Figure 2). Annual implant loss was higher when implants were placed in a mixture of AB and BS compared with placement of implants in AB or BS

alone (0.81 versus 0.23,  $p < 0.001$ ; Figure 3). Implant loss per year was independent of simultaneous or delayed implant placement in relation to MSFA (0.38 versus 0.39,  $p > 0.05$ ; Figure 4) or dental status at time of implant placement (0.13 versus 0.23,  $p > 0.05$ , Figure 5).

## Discussion

Today, MSFA is commonly performed when the residual vertical alveolar bone height is  $\leq 6$  mm. Analysis of the included papers showed that MSFA predictably leads to high implant survival rates in both partially and fully edentulous patients. Irrespective of the grafting materials applied, MSFA is accompanied by high implant survival, limited peri-implant marginal bone loss and few overall complications. In one study, lower implant survival rate is reported, which might be due to the use of machined implants (Mordenfeld et al., 2014). Later studies commonly used implants with a roughened surface (Raghoobar et al., 2001; Nkenke & Stelzle, 2009; Pjetursson et al., 2008; ).

The included studies used various graft healing periods and time frames between MSFA and start of prosthetic loading. This variety in approaches hampers generalization of the results. Therefore, it was not possible to draw conclusions about the optimal healing time of the graft material and implants before loading after MSFA with AB, BS or a mixture of AB and BS. Nevertheless, considering the more favourable survival rates after longer graft healing times, a prolonged healing period before implant placement seems advisable if BS or a mixture of BS and AB is used. This presumption is supported by studies reporting that bone-to-implant contact and volumetric stability of the graft material early after MSFA with AB or a combination of AB with BS is higher than when solely BS was used (Jensen et al., 2013). The obtained results from this systematic review revealed that implant loss was highest in studies in which a mixture of AB and BS was used. Presumably, this result is due to the outlier in the studies applying a mixture, namely the study in which implants were simultaneously placed with the MSFA and loaded after six weeks (Cannizzaro et al., 2013). It is therefore suggested that –assuming a sufficiently long healing period– implant survival in areas reconstructed with a mixture of AB and BS is comparable with implants placed in areas reconstructed with AB or BS alone.

In both studies with a 5-year and 10-year follow up, peri-implant marginal bone loss after MSFA was well within acceptable limits and mainly occurred during the early healing phase (Aghaloo et al., 2016; Starch-Jensen et al., 2018). When using BS or a mixture of AB with BS, less volumetric dimensional change occurs when compared to the use of AB alone (Shanbhag, Shanbhag, & Stavropoulos, 2014). Two other studies showed that volumetric resorption of AB did not compromise implant placement or implant survival (Boven et al., 2017; Slot et al., 2018) and that long-term changes in the augmented sinus height were minimal, irrespective of the grafting material used (Starch-Jensen & Jensen, 2017). An important limitation, however, is that the results of the studies described in the current review were all based on two-dimensional quantifications, while the changes occurring in grafted regions are three-dimensional.

PROMs are essentially subjective reports of patient perceptions. Understanding the influence of various prosthodontic rehabilitation options on orofacial aesthetics, chewing function and oral health-related quality of life is an important prerequisite for selecting of the best rehabilitation procedure with the highest treatment effect and lowest morbidity for patients (Boven et al., 2017). The Oral Health Impact Profile Questionnaire, Orofacial Esthetic Scale and Chewing Function Questionnaire are common PROM methods, although the specificity of these methods is unclear (Vervoorn, Duinkerke, Luteijn, & van de Poel, 1988). The two studies that used PROMs reported favourable outcomes after MSFA, irrespective of the prosthodontic concept applied (Boven et al., 2017; Slot et al., 2018).

Intra- and postoperative complications, including prosthetic complications, were uncommon, but the few reported complications were generally infrequent and not severe. In the included articles mostly only failure of the restoration was reported as technical complication. In only two articles also some other technical complications were reported (Cannizzaro et al., 2013; Slot et al., 2018). It is not clear whether in the other nine studies also technical complications took place. Perforation of the sinus membrane was the most frequent intraoperative complication. Two studies concluded that the presence of sinus septa and a low residual bone height (<6mm) are main risk factors for sinus membrane perforation (Schwarz et al., 2015; Tükel & Tatli, 2018). However, this review revealed that sinus membrane perforations or other intra/postoperative complications related to MSFA (wound dehiscence or infections) did not decrease implant survival. The latter is probably due to the infrequent occurrence of such complications and the usually appropriate approach to cover perforations.

Regarding prognosis and survival outcomes, there were several shortcomings in the design of clinical studies and RCTs reporting on MSFA. For example, many studies on survival of implants placed in sinus grafted sites failed to report the original residual bone height at the site of presumptive implant placement; or it was unclear in which bone the implants were placed. Therefore these studies were not included. Another issue that needs to be considered in future RCTs is to include power analysis in the design of the studies.

Furthermore, depending on the size of the defect, this review indicates that BS might be as effective as AB and serve as an alternative with less morbidity (Al-Nawas & Schiegnitz, 2014; Rickert, Slater, Meijer, Vissink, & Raghoobar, 2012). Unfortunately, no long-term follow up studies with augmentation procedures applying BS have been conducted for the fully edentulous maxilla.

The costs of MSFA are also an important issue. Harvesting AB increases the operating time. Especially in case of extraoral donor sites, surgery is performed under general anaesthesia. In some studies the patients even had to be hospitalized (Boven et al., 2017; Slot et al., 2018). The additional costs of increased operating time, general anaesthesia, and hospitalization that are required for harvesting AB may exceed the costs of the BS by far. Detailed incremental cost-effectiveness analyses are needed to clarify this aspect. Such cost-benefit analyses should include not only costs derived from the surgical procedure, but also costs for future failures and complications (Thoma et al., 2015).

It has been suggested that membranes tend to increase bone formation and have a positive effect on implant survival (Pjetursson et al., 2008; Mordenfeld et al., 2014). A more recent systematic review did not support the positive effect of applying membranes with regard implant survival after bone augmentation. It was concluded that survival was not dependent on the use of a membrane (Jonker, Roeloffs, Wolvius, & Pijpe, 2016). A two-arm and split-mouth RCT also reported no differences in implant survival rates between membrane-covered and uncovered groups (Garcia-Denche et al., 2013). Thus, the presumed benefit of membranes on formation of vital bone remains questionable and requires further research.

With regard to large defects, more standardised studies are needed to better understand the clinical efficacy and limitations of BS; this would enable the most predictive graft selection for extensive cases. As such, future RCT studies should define defect size, augmented volume and regenerative capacity of the defects. Another topic for future research is transcrestal sinus membrane elevation an alternative for MSFA. This technique is a predictable and reliable approach to oral rehabilitation of the atrophic posterior maxilla and is accompanied by a high implant survival rate when used in cases with a residual bone height  $\geq 6$  mm (Tan, Lang, Zwahlen, & Pjetursson, 2008; Starch-Jensen & Jensen, 2017).

## Conclusions

Despite the lack of RCTs and the variety of approaches used in the prospective cohort studies, this review shows that MSFA (lateral window technique) is a safe and predictable procedure as part of oral rehabilitation of severely atrophic maxillae with dental implants. The survival of implants is high, with no difference in simultaneous or delayed implant placement, dental status being partially or fully edentulous, or using AB or BS as augmentation material.

## Acknowledgement

We like to thank dr. Konstantina Delli for her help with the statistical analyses.

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**TABLE 1** Patient and treatment characteristics

Author et al. (year)	Setting: institution(I) or private(P)	No. patients	Males/females	Age range (yrs)	Mean age (yrs)	Residual bone height (mm)	No. Sinuses	Smokers	Partially/Fully edentulous	1 or 2 stage surgery	Antibiotic prophylaxis (Y/N)	Trapdoor / access hole	Sinial membrane coverage	Graft material	Implant brand/type	No. Implants	Fixed restoration or overdenture	Follow-up (yrs)	Dropout (%)
Bornstein et al. (2008)	I	56	22/34	19-74	53.9	<4	59	0	56/0	2	Y	35/21	RCM	1:1 AB-DBBM or 1:1 AB- $\beta$ -TCP	Straumann SLA/TPS	111	fixed	5	10.7
Özkan et al. (2011)	I	28	12/16	28-60	49.6	4-6	42	NR	28/0	1	NR	42/0	RCM	DBBM	ITI/Camlog	59	fixed	5	0.0
Cricchio et al. (2011)	I/P	10	5/5	17-68	45.2	<6	11	1	10/0	1	Y	11/0	None	None	Nobel Biocare TiUnite	19	fixed	5	0.0
Oliveira et al. (2012)	P	10	3/7	35-62	52.1	<4	13	NR	10/0	2	Y	13/0	RCM	DBBM	Straumann SLA	24	fixed	9	0.0
Dasmah et al. (2013)	I	19	2/17	35-75	58.0	2-5	38	1	0/19	2	Y	38/0	NR	AB with or without PRP	Astra Tech	76	fixed	5	26.7
Cannizzaro et al. (2013)	P	20	6/14	30-72	53.3	3-6	20	7	17/3	1	Y	20/0	None	1:1 AB:DBBM	Zimmer Dental	44	fixed	5	15.0
Mordenfeld et al. (2014)	I	20	6/14	48-69	62.0	<5	30	9	18/2	2	Y	30/0	NR	1:4 AB:DBBM	Nobel Mark II (machined)	79	fixed	10	30.0
Mordenfeld et al. (2016)	I	11	5/6	50-79	67.0	<5	22	NR	2/9	2	Y	22/0	RCM	DBBM or BCP	Straumann SLA	47	fixed	5	0.0
Khoury et al. (2017)	P	118	47/71	32-69	56.3	<6	198	41	118/0	1/2	Y	198/0	NRTM	Phycogenic HA liner + AB	Xive S	578	fixed	10	8.5
Boven et al. (2017)	I	25	10/15	42-74	59.1	<5	50	0	0/25	2	Y	50/0	None	AB	Straumann SLA	150	ODBC	5	8.0

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jcpe.13055

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Slot et al. (2018)	I	66	33/33	34-77	60.2	<5	132	0	0/66	2	Y	132/0	None	AB		Straumann SLA	330	ODBC	5	9.1
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AB: autogenous bone

BCP: synthetic biphasic calcium phosphate

DBBM: deproteinized bovine bone mineral

NRTM: non-resorbable titanium membrane

ODBC : Overdenture bar-connection

Phycogenix HA: Phycogenic hydroxyapatite

PRP: Platelet-rich plasma

RCM: resorbable collagen membrane

$\beta$ -TCP: synthetic porous  $\beta$ -tricalciumphosphate

**TABLE 2** Outcome measures and complications

Author et al. (year)	Graft material	No. implants	No. Sinusses	Follow-up (yrs)	No. failures	Before/after loading	Survival	Mean marginal bone loss	Complications								PROMs			
									No. Perforations Schneiderian membrane	No. Post-op Bleedings	No. Post-op infections	Abscess	Sinusitis	Peri-implant mucositis	Pain	Peri-implantitis	Failed restoration	PES	WES	VAS
Bornstein et al. (2008)	All groups§	111	59	5	2	0/2	98.20%	0.3 ± NR	18	2	1	0	0	0	2	2	0	NR	NR	NR
Özkan et al. (2011)	DBBM	59	42	5	0	0/0	100.00%	0.3 ± 0.7*	NR	NR	NR	NR	NR	NR	NR	NR	0	NR	NR	NR
Cricchio et al. (2011)	None	19	11	5	1	0/1	95.00%	2.4 ± NR	3	0	0	0	0	0	0	0	0	NR	NR	NR
Oliveira et al. (2012)	DBBM	24	13	9	0	0/0	100.00%	NR	0	0	0	0	0	0	0	0	0	NR	NR	NR
Dasmah et al. (2013)	All groups§	76	38	5	2	2/0	97.37%	0.7 ± 0.1*	12	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Cannizzaro et al. (2013)	1:1 AB:DBBM	44	20	5	5	5/0	88.64%	0.7 ± 0.4	2	0	2	1	1	1	0	0	0	NR	NR	NR
Mordenfeld et al. (2014)	1:4 AB:DBBM	79	30	10	5	3/2	93.67%	1.5 ± 0.9	9	NR	2	0	0	0	0	0	1	NR	NR	NR
Mordenfeld et al. (2016)	DBBM	23	11	5	2	1/1	91.30%	0.5 ± 0.7	NR	NR	NR	0	0	0	0	1	0	NR	NR	NR
	BCP	24	11	5	2	0/2	91.67%	0.7 ± 1.1	NR	NR	NR	0	0	0	0	2	0	NR	NR	NR
Khoury et al. (2017)	Phycogenic	578	198	10	3	0/3	99.48%	NR	21	62	0	0	0	12	0	8	0	NR	NR	NR

HA:AB																				
Boven et al. (2017)	AB	150	50	5	1	1/0	99.33%	0.7 ± NR	9	2	0	NR	NR	NR	NR	NR	1	NA	NA	8.5
Slot et al. (2018)	AB	330	132	5	1	1/0	99.70%	0.6 ± 0.6	25	4	0	0	0	5	0	8	3	NA	NA	8.7

- \*: mean marginal bone loss included implants in residual bone
- §: no distinction between graft groups
- AB: autogenous bone
- BCP: synthetic biphasic calcium phosphate
- DBBM: deproteinized bovine bone mineral
- NA: Not applicable
- Phycogenic HA: phycogenichydroxyapatite
- PRP: Platelet-rich plasma
- β-TCP: synthetic porous β-tricalciumphosphate

## Legends

Figure 1. Algorithm of study selection procedure.

Figure 2. Forest plot for cumulative weighted implant loss rate (%implant loss per year) meta-analysis for the studies.

Figure 3. Forest plot for cumulative weighted implant loss rate (%implant loss per year) comparing AB (group 1), BS (group 2) and AB/BS (group 3).

Figure 4. Forest plot for cumulative weighted implant loss rate (%implant loss per year) comparing simultaneous (group 1) or delayed implant placement (group 2).

Figure 5. Forest plot for cumulative weighted implant loss rate (%implant loss per year) of all studies with a dentate (group 1) or fully edentulous maxilla (group 2).

Table 1. Patient and treatment characteristics of the studies included for analysis

Table 2. Outcome measures and complications

## Legends

Supplementary figure 1. Risk of bias assessment of the non-randomized studies.

Supplementary figure 2. Risk of bias assessment of the randomized studies.



## Flow diagram



